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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/229,229	01/12/99	WAHL	G

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EXAMINER	
HOLLERAN, A	
ART UNIT	**PAPER NUMBER**
1642	13

DATE MAILED: 07/31/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/229,229	Wahl et al
Examiner	**Group Art Unit**
Anne Holleran	1642

☒ Responsive to communication(s) filed on *May 1, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-27* is/are pending in the applicat

Of the above, claim(s) *5-27* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7, 8*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 1-4 in Paper No. 10, filed May 1, 2000, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

2. Applicant's claim to priority of provisional applications 60/071,146 and 60/077,644 under 35 U.S.C. 119(e) is acknowledged.

Claim Rejections - 35 USC § 112

3. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying agents which induce reduction or elimination of DM or extrachromosomal DNA by measuring micronuclei formation, does not reasonably provide enablement for making and using methods for identification of therapeutic agents which induce cell maturation or cell death by measuring levels of DM or extrachromosomal DNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

Claims 1-4 are drawn to methods for identifying therapeutic agents which induce cell maturation or cell death. Cell maturation or cell death are broadly defined in the specification as including apoptosis, necrosis, or any other means of preventing cell division, reduced tumorigenicity, loss of pharmaceutical resistance, maturation, differentiation or reversion of the neoplastic phenotype of cells (page 10, lines 20-23).

The methods of claims 1-4 comprise the steps of contacting test cells with a potential therapeutic agent wherein the test cells contain established levels of DM or extrachromosomal DNA and are capable of undergoing micronucleation; and of assaying the test cells for the level of DM or extrachromosomal DNA whereby reduction or elimination of DM or extrachromosomal DNA indicates that the agent is a therapeutic agent that promotes micronucleation which results in cell maturation or cell death. Claim 2 adds the limitation that the test cells lack functional tumor suppressor protein. Claim 3 adds the limitation that the test cells contain an oncogene and claim 4 adds the limitation that the assay of DM or extrachromosomal DNA levels is done by FISH, flow cytometry, centrifugal fractionization, or histone-GFP labeling. Thus, the methods of claims 1-4 are drawn to methods using any type of test cell, and in some embodiments, the test cells either lacks functional tumor suppressor protein or contains an oncogene.

The specification teaches how to perform assays for measurement of micronuclei containing DM sequences and the specification describes methods for identifying agents which have the ability to reduce levels of DM or extrachromosomal DNA through the induction of micronucleation. However, the specification does not provide teachings that would enable one of skill in the art to correlate a method of identifying agents which reduce DM or extrachromosomal DNA through induction of micronucleation with the identification of therapeutic agents, given the broad definition of the potential actions of the identified therapeutic agents (page 10, line 20-23). For example, the specification provides no teachings to correlate the elimination of DM or extrachromosomal DNA with reversion of the neoplastic phenotype of the cell. Even if the claimed methods were limited to methods employing test cells containing amplified oncogenes, wherein the amplified oncogenes were present within DM or extrachromosomal DNA, it is not clear from the specification that the claimed methods would result in the identification of therapeutic agents which would reverse the neoplastic phenotype because the neoplastic phenotype is determined by a plurality of factors; the over amplification of oncogenes is just one factor contributing to the neoplastic phenotype.

Therefore, the claimed methods are not supported by a specification that enables one of skill in the art to practice the claimed methods commensurate in scope with the claimed methods.

5. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a method of identifying therapeutic agents which induce cell maturation or cell death. The claimed methods lack an adequate correlation step because the correlation step is not of the same scope as the preamble of the claim. The correlation step is the analysis of DM or extrachromosomal DNA whereby reduction of DM or extrachromosomal DNA indicates that the agent is a therapeutic agent that promotes micronucleation which results in cell maturation or cells death. However, the preamble is not limited to the identification of therapeutic agents which induce cell maturation or cell death and is not limited to an assay for identifying therapeutic agents which induce cell maturation or cell death by induction of micronucleation.

Claim 1 is also vague and indefinited because the claimed methods comprise a step of assay for levels of DM or extrachromosomal DNA. However, the specification only describes methods of measuring DM or extrachromosomal DNA that exists within micronuclei as a method to identify therapeutic agents.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Tometsko (U.S. Patent 5,229,265; published Jul. 20, 1993).

The subject matter of claims 1 and 4 have been discussed above. Claims 1 and 4 may be interpreted to be drawn to methods for the identification of agents which induce cell maturation or cell death by induction of micronuclei. As micronuclei by definition contain extrachromosomal DNA, a method the employs steps of measuring micronuclei is a method that comprises a step of measuring extrachromosomal DNA.

Tometsko discloses methods of identifying clastogenic agents which are agents which induce the fragmentation of chromosomes. The methods comprise assaying micronuclei formation in mouse blood cells by flow cytometry (see abstract). Tometsko provides an example of the disclosed methods to assess clastogenicity in cyclophosphamide (col. 22, line 43 - col. 23, line 12). Thus, Tometsko discloses a method that is the same as that claimed.

7. Claims 1 and 4 are rejected under 35 U.S.C. 102(e) as being anticipated by Dertinger et al (U.S. Patent 5,858,667; published Jan. 12, 1999; filed Sep. 6, 1996).

Dertinger et al discloses a method of identifying clastogenic agents by assaying micronuclei by single laser flow cytometry (abstract and col. 3, lines 21-24). Thus, Dertinger et al discloses a method that is the same as that claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

ALH

Anne L. Holleran
Patent Examiner
July 17, 2000

Yvonne Eyler

YVONNE EYLER, PH.D
PRIMARY EXAMINER